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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/001,227	11/30/2001	Rosana Kapeller-Libermann	MNI-199	8456

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EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 06/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/001,227	KAPELLER-LIBERMANN ET AL.	
	Examiner	Art Unit	
	Jon M. Lockard	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35,38-40,43 and 46-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35,38-40,43 and 46-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/17/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S.O.O.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. The Amendment filed 17 March 2005 has been received and entered in full. Claims 36-37, 41-42, 44-45, and 49-66 and claims 35, 40, 43, and 48 have been amended. Therefore, claims 35, 38-40, 43, and 46-48 are pending and the subject of this Office Action.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

3. The Information Disclosure Statement (IDS) submitted on 17 March 2005 has been considered by the Examiner.

Withdrawn Objections and/or Rejections

4. The objection to the drawings as set forth at page 4 (¶11) in the previous Office Action (mailed 15 November 2004) is withdrawn in view of Applicant's amendments (filed 17 March 2005).

5. The objection to the Specification as set forth at page 4 (¶12) in the previous Office Action (mailed 15 November 2004) is withdrawn in view of Applicant's amendments (filed 17 March 2005).

6. The objection to claims 40, 48, 56, and 64 as set forth at page 4(¶13) in the previous Office Action (mailed 15 November 2004) is withdrawn in view of Applicant's amendment of claims 40 and 48 and cancellation of claims 56 and 64 (filed 17 March 2005).

7. The rejection of claims 35-66 under 35 U.S.C. §112(2), as set forth at page 5 (¶14-17) in the previous Office Action (mailed 15 November 2004) is withdrawn in view of Applicants amendment of claims 35 and 43 which deleted the terms "pain disorder" and "pain signaling mechanism", respectively, and cancellation of claims 51 and 59 (filed 17 March 2005).

8. The rejection f claims 35-66 under 35 U.S.C. §112, 1st Paragraph as failing to comply with the enablement requirement as set forth at pages 5-8 (¶18-24) in the previous Office Action (mailed 15 November 2004) is withdrawn in view of Applicants amendment of claims 35 and 43 which deleted the terms "pain disorder" and "pain signaling mechanism", respectively, and cancellation of claims 36-37, 41-42, 44-45, and 49-66 (filed 17 March 2005). However, a new grounds of rejection has been applied below.

9. The rejection of claims 35-36, 38-44, 46-52, 54-60, and 62-66 under 35 U.S.C. §102(e) as being anticipated by Baughn et al., as set forth at pages 9-10 (¶25-27) in the previous Office Action (mailed 15 November 2004) is withdrawn in view of Applicant's amendment of claims 35 and 43 which now recite that the methods are carried out in specific cell types, namely "a brain cell, a cell derived from the spinal cord, and a cell derived from dorsal root ganglion", and cancellation of claims 36, 41-42, 44, and 49-52, 54-60, and 62-66 (filed 17 March 2005).

Maintained and New Objections/Rejections

Claim Rejections - 35 USC § 112, 1st Paragraph (Enablement)

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 35, 38-40, 43, and 46-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

12. Claims 35, 38-40, 43, and 46-48 are directed to a method for identifying a candidate compound capable of binding to a carboxylesterase polypeptide. However, the instant specification fails to teach how to achieve the proposed binding assay, thus requiring undue experimentation of one skilled in the art to use the claimed invention with a reasonable expectation of success.

13. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

14. It is known and described in the prior art that mammalian carboxylesterases represent a multigene family, the products of which are localized in the endoplasmic reticulum of many tissues (See Satoh et al., (1998). "The mammalian carboxylesterases: from molecules to functions". Annual Reivew of Pharmacology and Toxicology 38:257-288, see especially pages 257 and 268). Furthermore, the Specification teaches that it is predicted that human COE-2

(SEQ ID NO:2) of the Instant Application is localized in the mitochondria (52.2%), cytoplasm (13.0%), vacuolar bodies (8.7%), extracellular space and cell wall (8.7%), endoplasmic reticulum (8.7%), golgi apparatus (4.3%), and in the peroxisomal bodies (4.3%) (shown as percent probability). However, the art teaches that the ability to deliver proteins into cells, where one of skill in the art would expect the COE-2 protein (SEQ ID NO:2) to be localized, is problematic due to the bioavailability restriction imposed by the cell membrane. The plasma membrane of cells forms an effective barrier which restricts the intracellular uptake of molecules to those which are sufficiently non-polar and smaller than approximately 500 daltons in size (See Wadia et al. (2003). "Modulation of cellular function by TAT mediated transduction of full length proteins". Current Protein and Peptide Science. 4:97-104). Therefore, one skilled in the art would not know, with any level of predictability, that a method comprising combining a compound with a sample comprising a cell expressing the COE-2 polypeptide (SEQ ID NO:2) would result in the binding of the compound to the COE-2 polypeptide.

15. The instant specification also fails to disclose sufficient information on how to assess the binding of the candidate compound to the COE-2 polypeptide (SEQ ID NO:2). In the absence of this guidance, a practitioner would have to resort to a substantial amount of undue experimentation to practice the invention using the specification and the state of the prior art as outlined above.

16. There are no working examples presented in the instant specification that describe compounds which bind to the COE-2 polypeptide (SEQ ID NO:2). The specification fails to disclose whether or not candidate compounds can be targeted to the COE-2 polypeptide, which based on the teachings of the prior art and the instant specification, is located intracellularly.

Therefore, the person of ordinary skill in the art would not be able to use the method to identify a candidate compound capable of binding to a COE-2 polypeptide because there is no reasonable expectation that compounds could be targeted to the intracellular protein and the specification as filed has not provided any guidance on how to assess the binding of the candidate compound to the COE-2 polypeptide. In order to practice the invention using the specification and the state of the prior art as outlined above, the quantity of experimentation required to practice the invention as claimed would be undue. A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentech, Inc, v. Novo Nordisk*, 42 USPQ 2d 100, (CAFC 1997), the court held that:

"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable", and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[I]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

17. Thus, in view of the lack of teachings and unpredictability of the art set forth above and the total absence of working examples, the instant specification is not found to be enabling for a method for identifying a candidate compound capable of binding to a COE-2 polypeptide. It

would require undue experimentation and making a substantial inventive contribution for the skilled artisan to discover how to use the Applicants' invention as currently claimed.

Summary

18. No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback**, can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

JML
May 25, 2005

Bridget E. Bunner
patent examiner